REMARKS

Introduction

It is respectfully requested that this Amendment After Final Rejection be entered and made of record. It is believed that the following amendments and remarks place the application in a form for allowance. The following amendments and remarks at least place the claims in a better form for appeal. No new matter is presented, as such the amendment is proper under 37 C.F.R. § 1.116.

Request for Withdrawal of Final Rejection

As a preliminary matter, it is respectfully submitted that the Examiner's final rejection of the application was premature.

MPEP §706.07(a) states, in part:

> A second or any subsequent action on the merits in any application or patent involved in reexamination proceedings should not be made final if it includes a rejection, on prior art not of record, of any claim amended to include limitations which should reasonably have been expected to be claimed. See MPEP § 904 *et seq.* (emphasis supplied).

MPEP § 904 addresses how the examiner should search the application. Specifically, Section 904 states that:

> The first search should be such that the examiner need not ordinarily make a second search of the prior art, unless necessitated by amendments to the claims by the applicant in the first response,... It should cover the invention as described and claimed, including the inventive concepts toward which the claims appear to be directed. (emphasis supplied).

In the final rejection, the Examiner states that "Applicant's amendments to the claims necessitated the new ground(s) of rejection presented in the Office action." However, the only amendments made to Applicant's claims were to add the provision in the preamble of claim 10 that Applicant's method results in a reduction in the number of verotoxin-producing organisms in

the colon of animals. Claim 10 was further amended to specify that the polyclonal, monospecific antibodies are to verotoxin-producing organisms and their toxins. These claim amendments would have reasonably been expected to be claimed since their subject matter was extensively described throughout the specification, as well as in the originally filed dependent claims.

For instance, the Summary of the Invention specifically states that the invention describes an animal serum composition "containing polyclonal, monospecific antibodies against Shigella, E. coli 0157:H7 and other VTEC which is administered to animals to protect their gastrointestinal health....". (Spec. p. 7, second para.). The Summary further states that the antibodies are "specific to both the organism and verotoxins, including endotoxin, SLT-I, and SLT-II, ...". (Spec. p. 7, second para.). Further, former claim 5 (now canceled) stated that the concentration of monospecific antibodies was sufficient "to achieve a verotoxin neutralization titer of equal to greater than 1:8."

Claims 21-24 were also added to the application with Applicant's January 11, 2001 amendment. However, these claims include all of the same subject matter that had already been described in the original claims filed with the application.

Therefore, since the limitations added to claim 10 and the subject matter of new claims 21-24 were described throughout the specification and originally filed claims, the examiner's initial search of the art should have included art relevant to the claimed invention as amended in the January 11, 2001 response in accordance with MPEP § 904. For this reason, the limitations placed in Applicant's claims in his last response would have been reasonably expected to be claimed under MPEP § 706.07(a). Since the Examiner's final rejection includes prior art not previously made of record, the final rejection is premature. Applicant therefore respectfully requests that it be withdrawn.

In addition, Applicant would respectfully note that in Paper No. 7, the Examiner specifically stated that, "The claimed method of prevention of verotoxin-induced disease appears to be free of the prior art." (Page 4, para. 7). If this was the case for the claims as filed, then it would certainly held true for the claims as amended. Applicant relied to his detriment on the

Examiner's previous statement that the claimed invention was "free of prior art" since, had the references been cited in the first Office Action, Applicant would have had a fair opportunity to have his arguments made of record as a matter of right. It would be inequitable to penalize Applicant on the basis of the Examiner's delay in citing the prior art references.

Applicant therefore respectfully requests that the final rejection be withdrawn.

Claim Rejections - 35 U.S.C. 102(b)

Claims 10-12, 14-17, and 22-23 were rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,512,282 (Krivan et al.), U.S. Patent No. 4,096,244 (Newson), or U.S. Pat. No. 4,623,541 (Elliot et al.).

Claims 10 (from which claims 11-12 and 14-17 ultimately depend) and claim 23 have been amended to include the provision of claim 21 (now canceled) whereby the polyclonal, monospecific antibodies are present in a concentration to achieve a verotoxin neutralization titer of equal to or greater than 1:8. Since claim 21 was not included in the Examiner's anticipation rejection, it is respectfully submitted that claims 10-12, 14-17 and 23 are not anticipated by Krivan, Newson, or Elliot.

Claim 22 has been amended to include the provision of claim 13 whereby the composition is administered in a dose of from about 1 g to about 30 g of plasma protein per day. Since claim 13 was also not the subject of the Examiner's anticipation rejection, it is respectfully submitted that claim 22 is not anticipated by Krivan, Newson, or Elliot.

Claim Rejections - 35 U.S.C. 103

The Examiner has rejected claims 13, 21, and 24 as being unpatentable over U.S. Pat. No. 4,096,244 (Newson) or U.S. Pat. No. 4,623,541 (Elliot) under 35 U.S.C. 103(a). The Examiner notes that the references differ from the claimed invention in that they do not teach the administration of the serum composition in a dose of about 1-30 g per day nor the administration of the composition comprising a neutralization titer of greater than 1:8. The Examiner then asserts, however, that "the optimization of dosages and titers are obvious and routine in the art"

and, thus, the optimization "would fall well within the purview of one of skill in the art." Applicant respectfully traverses this rejection.

As noted above, the claims as amended all include either the provisions of claim 13 or 21 (now canceled). Applicant will therefore address the rejection with respect to all of claims 10-17 and 22-24.

The PTO bears the burden of establishing a case of prima facie obviousness. In re Fine, 837 F.2d 1071, 1074 (Fed. Cir. 1988). It is axiomatic that in order to establish a prima facie case of obviousness, it is necessary for the examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied prior art, that one having ordinary skill in the art would have been led to combine the relevant teachings of the applied references in the proposed manner to arrive at the claimed invention. See e.g. Carella v. Starlight Archery, 804 F.2d 135 (Fed. Cir. 1986); Ashland Oil, Inc. v. Delta Resins & Refractories, Inc., 776 F.2d 281 (Fed. Cir. 1985). This suggestion cannot stem from the applicant's own disclosure, however. In re Ehrreich, 590 F.2d 902 (CCPA 1979).

The Examiner's obviousness rejection is based on the premise that it would have been obvious to have modified the doses and titers described in Newson and Elliot in order to arrive at those of Applicant's claimed invention. The Federal Circuit, however, has consistently rejected "obvious to try" as a legitimate test of patentability. See e.g. In re Fine, 837 F.2d 1071, 1075 (Fed. Cir. 1988). It is therefore respectfully submitted that the Examiner has not established a prima facie case of obviousness.

In In re Antonie, 559 F.2d 618 (CCPA 1977), the CCPA (the predecessor to the Federal Circuit) discussed how the obvious to try ban should apply to inventions in which the inventor has "optimized" quantitative or other variables in a prior art structure or process. There, the invention at issue was a waste water treatment device in which wastewater passed through a tank in which contactors continuously rotate. Id. The primary prior art reference, El-Naggar, showed the device's basic structure but was "silent regarding quantitative design parameters". Id. El-Naggar did state that output purity (referred to as "efficiency") could be increased to 95% by

increasing the area of the contactor. Id. The applicants claimed the device with "a ratio of tank volume to contactor area of 0.12 gal./sq. ft." Id. They asserted that this volume-contractor ratio maximizes "treatment capacity" in that a lower value gives lower capacity and a higher value increases costs without increasing capacity. Id. The Patent Office rejected the applicants' claims on the basis that while the ratio to tank volume to contactor area of 0.12 gal./sq. ft. was not disclosed in El-Naggar, it would have been obvious for one skilled in the art to have optimized this value. Id. at 619.

The Court reversed the Patent Office's rejection. Antonie, 559 F.2d at 620. While the Court noted that the discovery of an optimum value of a variable in a known process is normally obvious, a primary exception lies in cases where the results of optimizing a variable, which was known to be result effective, were unexpectedly good. Id. The Court further stated that another exception lies "in which the parameter optimized was not recognized to be a result-effective variable." Id. Therefore, since the El-Naggar reference did not disclose or suggest the functional relation of treatment capacity to tank volume-to-contactor area, the Court held that the PTO's assumption that El-Naggar suggested experimentation with the constant tank volume as optimized and claimed by the applicants was not reasonable. Id. The majority of the Court dismissed the PTO's position that "it would always be obvious for one of ordinary skill in the art to try varying every parameter of a system in order to optimize the effectiveness of the system even if there is no evidence in the record that the prior art recognized [that] that particular parameter affected the result." Id. The Court noted:

> As we have said many times, obvious to try is not the standard of 35 U.S.C. § 103...Disregard for the unobviousness of the results of "obvious to try" experiments disregards the "invention as a whole" concept of § 103,...and overemphasis on the routine nature of the data gathering required to arrive at appellant's discovery, after its existence became expected, overlooks the last sentence of § 103.

Id.

Similarly, in the Rijckaert case, the Federal Circuit held that the PTO failed to establish a prima facie case of obviousness for a video recording and reproducing apparatus signal processing circuit in which the time expansion and compression were by a factor of two. In re Rijckaert, 9 F.3d 1531, 1533-34 (Fed. Cir. 1993). The PTO reasoned that recognition of the claimed relationship was "the mere discovery of a relationship that is applicable to [a] prior art apparatus[, and] does not [give] rise to a patentable invention." Id. The Federal Circuit disagreed, stating that the PTO erred because the primary reference disclosed neither the wrapping angle variable nor the recording occurrence variable (M), (2) did not "discuss the claimed relationship of the three variables to time expansion/compression", and (3) did not "describe the use of time expansion and compression as a means of optimally filling tracks." Id. The Court further stated that:

> While the condition described may be an optimal one, it is not "inherent" in [the primary reference]. Nor are the means to achieve the optimal condition disclosed [by the reference], explicitly or implicitly. "The mere fact that a certain thing may result from a given set of circumstances is not sufficient [to establish inherency.]"..."That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown."

Id. at 1534.

In the instant case, Newson and Elliot are cited for their teaching of a method of internally administering a composition to an animal which comprises polyclonal, monospecific antibodies isolated from the animal serum. (Office Action pp. 2-3). Newson discloses the administration of a dried particulate serum containing active immunoglobulins which is suitable for administration to newborn piglets. (Col. 2, lines 6-10). The Newson composition is administered in an amount ranging from about 75 to about 125 parts by weight per 100 parts by weight of the basic milk powder. (Col. 4, lines 36-39).

Similarly, Elliot discloses a method of producing purified porcine or bovine immunoglobulins for use in the formulation of milk replacers for artificial rearing of neonatal

pigs to provide improved passive immunity to disease. (Col. 3, lines 6-11). Elliot discloses that such a composition should be administered to pigs at a level of 10 gm/kg body weight on day 1 and 2 gm/kg body weight on days 2-10 inclusive. (Col. 6, lines 18-20).

In this case, Applicant has discovered that when polyclonal, monospecific antibodies to verotoxin-producing organisms and their toxins are isolated from animal serum are administered to animals in a dose of from about 1-30 grams of plasma protein per day (claim 22) or in a concentration to achieve a verotoxin neutralization titer of equal to or greater than 1:8 (claims 10 and 23), the product is effective in reducing verotoxin concentrations in the colon. In contrast, Newson or Elliot are completely silent regarding any connection between administration of animal serum compositions and reduction in the number of verotoxin-producing organisms. Thus, the circumstances of this case clearly fall within those described in the Antonie and Rijckaert cases.

Since Newson and Elliot did not understand or appreciate the connection between the administration of polyclonal, monospecific antibodies to verotoxin-producing organisms and verocytotoxicity, persons skilled in the art would not have had any incentive, nor understood how to alter their described dosing levels in order to "optimize" their compositions' effectiveness against verotoxin-producing organisms. Thus, as in the Antonie and Rijchaert cases, Applicant's optimized parameter was not recognized by the primary references to be result-effective in reducing verocytotoxicity in animals. Hence, the Examiner's assumption that either Newson or Elliot suggested experimentation with the concentration of antibodies to achieve Applicant's optimum neutralization titer of equal to or greater than 1:8 or Applicant's optimized dose of 1-30 g of plasma protein/day is not reasonable.

In addition, Applicant has demonstrated that the results achieved in administrating polyclonal, monospecific antibodies to verotoxin-producing organisms in reducing verocytotoxicity were "unexpectedly good." As shown by Example 1 of the specification, while animals treated in this manner had verocytotoxicity levels ranging from 4-16, untreated animals had a verocytotoxicity level of 4096. Thus, animals treated with the claimed composition had

antitoxin activity at least 256 times greater than that of untreated animals. Thus, the claimed invention also falls within the other exception discussed in the Antonie case that negates a prima facie case of obviousness based on routine optimization of variables.

For all of these reasons, and in view of the binding authority of the Federal Circuit caselaw described above, it is respectfully submitted that the claimed invention is not rendered obvious by either or both of Newson and Elliot. Applicant therefore respectfully requests that this ground of rejection be withdrawn.

Conclusion

For the above-stated reasons, it is believed the application is in a prima facie condition for allowance. Allowance is respectfully requested.

No fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,

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AMENDMENT — VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims

Claims 10 and 22-23 have been amended as follows:

10. (Twice Amended)

A method of reducing the number of verotoxin-producing organisms in the colon of animals comprising:

internally administering a composition to an animal which comprises polyclonal, monospecific antibodies to verotoxin-producing organisms and their toxins isolated from animal serum; wherein the polyclonal, monospecific antibodies are present in a concentration to achieve a verotoxin neutralization titer of equal to or greater than 1:8.

Claim 21 has been canceled.

22. (Amended)

A method of reducing the number of verotoxin-producing organisms in the colon of animals selected from the group consisting of mammals and poultry comprising:

internally administering a composition to an animal selected from the group consisting of mammals and poultry, said composition comprising polyclonal, monospecific antibodies to verotoxin-producing organisms and their toxins;

said composition being isolated from animal serum;

wherein the composition is administered in a dose of from about 1 g to about 30 g of plasma protein per day.

23. (Amended)

A method of reducing the number of verotoxin-producing organisms in the colon of animals selected from the group consisting of mammals and poultry comprising:

internally administering a composition to an animal selected from the group consisting of mammals and poultry, said composition comprising polyclonal, monospecific antibodies to verotoxin-producing organisms and their toxins;

said composition being isolated from animal serum;

whereby the source of the animal serum is selected from the group consisting of bovine and porcine;

wherein the polyclonal, monospecific antibodies are present in a concentration to achieve a verotoxin neutralization titer of equal to or greater than 1:8.